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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,657	04/16/2001	Nathalie Garcon	B 45158	2235

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EXAMINER	
LUCAS, ZACHARIAH 15	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,657	GARCON, NATHALIE	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-37,39-62 and 71-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *46,56,115 and 118* is/are allowed.

6)☒ Claim(s) *32-45,47,50-62,71-114,116,117 and 119* is/are rejected.

7)☒ Claim(s) *42,48 and 49* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 32-37, 39-62, and 71-119 are currently pending in the present application. Claims 32-37, 39-41, 43-45, 50-62, and 71-114 were rejected in the prior office action (mailed September 10, 2002. Claim 42 was objected to, and not further treated on the merits as being an improper multiple dependant claim. Claims 46-48 and 115 were indicated to be allowable.

2. A response (Amend. D) to the prior action was filed by the applicant was received by the Office on January 16, 2003. This response cancelled claims 38, and 63-70; amended claims 32, 39-42, and 71-92; and added claims 116-119.

3. This action is being made Non-Final because new issues and rejections are being raised.

Specification

4. **(Prior Objection-Withdrawn)** The disclosure was objected to in the prior action because of the following informalities:

On page 4, lines 6-7 of the application, the specification read "the substantially free at immunostimulant." It appears that the word "at" should be substituted with "of." The applicant has so amended the specification. The Objection is therefore withdrawn.

5. **(New Objection)** The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction

of the following is required: The specification does not provide any antecedent basis for the claim limitation regarding immunostimulants "wherein the immunostimulant is not a saponin derived from the bark of Quillaja Saponaria Molina." It is suggested that a sentence such as the following be inserted at the end of the last paragraph of page 5: -- The immunostimulants of the vaccines of the present invention may be any immunostimulant, including those listed above, or may be any immunostimulant wherein the immunostimulant is not a saponin derived from the bark of Quillaja Saponaria Molina. -- Such an insertion would overcomes the present objection.

6. **(New Objection)** The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification does not provide any antecedent basis for the claim limitation "characterized in that said metallic salt is substantially free of monophosphoryl lipid A, or [a] derivative thereof." While the specification supports limitations to the claimed antigen/metallic salt complex that are substantially free of immunostimulant (page 3, lines 2-6), it does not support the limitation for a complex of an antigen and metallic salt wherein the any immunostimulant other than MPA may be adsorbed to the salt in addition to the antigen.

Claim Objections

7. **(Prior Objection-Withdrawn)** Claim 42 was objected to in the prior action under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must refer to the multiple claims from which it is depending in alternative form. See MPEP § 608.01(n). The

claim has been amended such that it now depends from claims 32-37 in the alternative forms. The objection is therefore withdrawn.

8. **(New Objection)** Claim 47 objected to because of the following informalities: the last phrase of the claim should read "or *a* derivative thereof," rather than "or derivative thereof." Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. **(Prior Rejection- Withdrawn)** Claims 32-37 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In claim 32, the claim limits the adjuvant composition to one wherein the immunostimulant is not a saponin derived from the bark of Quillaja Saponaria Molina." It is noted that there is support for such a limitation is the claims, but not the specification as filed. The rejection is therefore withdrawn, in view of the objection made above.

11. **(New Rejection-Necessitated by Amendment)** Claims 32-35, 39-43, 71, 72, 82, 83, 93, 94, 104, 105, 116, and 117 are rejected under 35 U.S.C. 112, first paragraph, as containing

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection. In the prior action, claims 32-37, 39-41, and 43-45, 50-62, and 71-114 were rejected for indefiniteness because the meaning of the term "other antigen" was not clear, as the term other appeared to focus on the claimed immunostimulants, thereby indicating that the immunostimulants may comprise antigens. It was suggested in that action that the claims be amended so a to clarify the distinction between the immunostimulants and the antigens. It was noted on page 5 of that action that an "immunostimulant is not introduced as an antigen, but as component to the vaccine designed to increase the efficacy of the antigen vaccine." It is now also noted that in the specification describing what is meant by an "immunostimulant," no reference is made to an antigen as an immunostimulant. App., page 5, lines 17-31. There is no indication in the specification or claims as filed that antigens themselves were considered to be immunostimulants according to the claimed invention, except for the unclear reference to the antigens of the claimed vaccines as "other antigens." As this reference was not made clear from the specification nor the claims, it would have been assumed that the applicant intended to exclude only antigens from binding the same adjuvant as the immunostimulant, and not that the immunostimulant itself was being considered as an adjuvant as these two components have different function in the claimed vaccines.

In an effort to overcome the indefiniteness rejection, the applicant amended claims 32 and 39, and written newly added claim 116 and 117 such that an immunostimulant may not be an antigen in itself. It is agreed that such would bring light to the term "other antigen," but as was

described in the prior action, and above, there is no support in the specification as filed for the assertion that an immunostimulant may itself be an antigen. Thus, the amendments to the claims introducing such matter in to the application constitute New Matter in the application. Claims 32, 39, 116, and 117, and the identified dependent claims are therefore rejected as reading on subject matter not described in the application as filed.

12. **(New Rejection-Necessitated by Amendment)** Claims 32-40, 42, 43, 116, and 117 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising an immunostimulant and an antigen, does not reasonably provide enablement for such compositions wherein said immunostimulant (first antigen) and said (second) antigen are the same. The claims have been described above. The claims are not enabled to the extent that they read on embodiments wherein the immunostimulant and the antigen are the same because the applicant has not demonstrated that any of the identified immunostimulants also have antigenic properties, or explained why one skilled in the art would immunize a person against an immunostimulant. Because the applicant has not shown that the immunostimulants are antigenic, and because the applicant has not shown why one skilled in the art would vaccinate a persons against the immunostimulants (therefore not showing one skilled in the art how to use such vaccines by not identifying a population to be treated) the applicant is not enabled for these claims.

13. **(New Rejection-Necessitated by Amendment)** Claims 32-35, 39-43, 71, 72, 82, 83, 93, 94, 104, and 105 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection. In the prior action, claims 32-37, 39-41, and 43-45, 50-62, and 71-114 were rejected for indefiniteness because the meaning of the term "other antigen" was not clear, as the term other appeared to focus on the claimed immunostimulants, thereby indicating that the immunostimulants may comprise antigens. The presently rejected claims have been amended to read on compositions comprising an immunostimulant and an (second) antigen, wherein the immunostimulant can be a first antigen, and wherein the first and second antigens can be the same. These claims further read on embodiments wherein the second antigen is one of the antigens described in, for example, claim 41. These claims lack support in the application as filed because the applicant has not demonstrated that any of these antigens may also act as immunostimulants.

14. **(New Rejection-Necessitated by Amendment)** Claims 32-35, 39-43, 71, 72, 82, 83, 93, 94, 104, and 105 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising an immunostimulant and an antigen, does not reasonably provide enablement for such compositions wherein said immunostimulant (first antigen) and said (second) antigen are the same. In the prior action, claims 32-37, 39-41, and 43-45, 50-62, and 71-114 were rejected for indefiniteness because the meaning of the term "other antigen" was not clear, as the term other appeared to focus on the claimed immunostimulants, thereby indicating that the immunostimulants may comprise antigens. The presently rejected claims have been amended to read on compositions comprising an immunostimulant and an

(second) antigen, wherein the immunostimulant can be a first antigen, and wherein the first and second antigens can be the same. These claims further read on embodiments wherein the second antigen is one of the antigens described in, for example, claim 41. These claims lack support in the application as filed because the applicant has not demonstrated that any of these antigens may also act as immunostimulants.

15. **(New Rejection)** Claims 39, 41-45, 50-55, 60-62, 71-74, 79-85, 90-96, 101-107, 112-114, 117, and 119 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vaccines, and methods of making the claimed vaccine composition, wherein the antigen is adsorbed to a separate metallic salt, does not reasonably provide enablement for such compositions where the antigen is not so adsorbed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The claims read on a vaccine composition, and a method of making such, wherein the composition comprises an immunostimulant adsorbed to a metallic salt, and an antigen, wherein the salt to which the immunostimulant is bound is substantially free of antigen. The applicant is not enabled for such claims because the applicant has not shown that antigen which is not bound by a separate metallic salt will not bind to the salt to which the immunostimulant is adsorbed. For example, Hauser (U.S. Patent 5,776,468 teaches that MPA will bind alum to which an antigen is already bound. Column 1, lines 45-53. It is therefore also likely that antigens that do not prevent immunostimulants from binding to salts to which they are bound, would also be able to bind to metallic salts to which such immunostimulants are already bound.

Further, the applicant has neither described any method of preventing such binding, nor identified and taught the use of immunostimulants that would inhibit such binding. As no such teachings or guidance are presented in the application, and as the art indicates that such may be a problem with the claimed compositions, the applicant is not enabled for such compositions or the processes of making them.

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. **(Prior Rejection-Maintained in part)** Claims 32-37, 39-41, and 43-45, 50-62, and 71-114 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Prior to entry of Amend. D into the record, the claims described a method of making a vaccine, or a vaccine, comprising "a) an adjuvant composition comprising an immunostimulant adsorbed onto a metallic salt particle, characterized in that the metallic salt particle is substantially free of other antigen, and b) an antigen." The claim referred to other antigens before the first antigen has been introduced. Thus, the claims were indefinite for lack of antecedent basis for the claimed term. Claims 32 and 39 have been amended such that the term "other antigen" has been removed, and the claims now read on a first and second antigen. However, because claim 44 still contains this language without an indication of the meaning of other antigen (as saponins have not been disclosed in the application to be antigens) the rejection

is maintained for this claim, and dependent claims 45, 50-52, 55, 60-62, 73, 74, 79-81, 84, 85, 90-92, 95, 96, 10-103, 106, 107, and 112-114.

18. **(New Rejection)** Claims 47 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 47 reads on a vaccine compositions comprising an immunostimulant adsorbed onto a metallic salt wherein said salt is free of antigen, and an antigen adsorbed onto a metallic salt, wherein said salt is free of monophosphoryl lipid A (MPA). It is unclear from the claim whether the claim includes embodiments wherein the antigen is adsorbed to a metallic salt to which a non-MPA immunostimulant is adsorbed, or if the claims intends to exclude all immunostimulant from the antigen/metallic salt complex.

19. **(New Rejection – Necessitated by Amendment)** Claim 73, 74, 79-81, 84, 85, 90-92, 95, 96, 101-103, 106, 107, and 112-114 are rejected for including limitations which lack antecedent basis in the claims. Claim 73, which depends from claim 44, will be treated as representative of the rejected claims. Claim 73 recites the limitation "A vaccine composition as claimed in [a prior claim], wherein the second antigen..." There is insufficient antecedent basis for the "second antigen" limitation in this claim. Claim 44, from which claim 73 depends, refers to the exclusion of an "other antigen," but does not describe a first or second antigen. It is therefore unclear what is meant by the term "second antigen."

20. **(New Rejection – Necessitated by Amendment)** Claims 75-81, 86-92, 97-103, 108-114 are rejected for including limitations that lack antecedent basis in the claims. Claim 75 is treated as representative of the rejected claims. Claim 75 recites the limitation "A vaccine composition as claimed in 46, wherein the second antigen..." There is insufficient antecedent basis for this limitation in the claim, because claim 46 already requires the presence of one antigen, but does not introduce a "second antigen." It is therefore unclear what is being claimed.

Allowable Subject Matter

21. Claims 46, 49, 53, 54, 56, and 115, and 118 are allowed. The subject matter of these claims appears to be free of the prior art. Although the art does teach the combination of the claimed immunostimulants and adjuvants, (see e.g. Hauser et al., U.S. Patent 5,776,468, col. 7, lines 27-39 (of record in the prior action), the art does not specifically teach adjuvant compositions wherein the antigen and immunostimulant are not bound to the same adjuvant molecules. See e.g., Hauser, col. 1, lines 45-53 (teaching that the immunostimulant reacts with the alum/antigen complex to form a single complex comprising all three elements).

Conclusion

22. Claims 53, 54, 48, and 49 are objected to as dependent on rejected claims.

23. The following prior art reference is made of record and is considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

So et al., U.S. Patent 5,817,314. This reference teaches vaccine compositions comprising a saponin adjuvant, and a second adjuvant- wherein the second adjuvant is preferably alum. Claims 3 and 4. The reference is not applied as art against the claims because the art teaches that the antigen is bound to alum, but does not require or teach that the saponin is bound to any metallic salt.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
March 24, 2003

JAMES HOUSEL 3/24/03
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